

# Prevalence of *Helicobacter pylori* infection in peptic ulcer perforations

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## Summary

**Background:** Most patients with chronic peptic ulcer disease have *Helicobacter pylori* (*H. pylori*) infection. In the past, immediate acid-reduction surgery has been strongly advocated for perforated peptic ulcers because of the high incidence of ulcer relapse after simple closure. Simple oversewing procedures either by an open or laparoscopic approach together with *H. pylori* eradication appear to supersede definitive ulcer surgery.

**Methods:** In 47 consecutive patients (mean age = 64 years, range 27-91) suffering from acute peptic ulcer perforation the preoperative presence of *H. pylori* (CLO test), the surgical procedure (laparoscopy or open surgery), the outcome of surgery, and the success of *H. pylori* eradication with a triple regimen were prospectively studied.

**Results:** Of these patients 73.3% were positive for *H. pylori*, regardless of the previous use of non-steroidal anti-inflammatory drugs (NSAIDs). Thirty-eight per cent underwent a simple laparoscopic repair. Conversion rate to laparotomy

reached a high of 32%. The main reasons for conversion were the size of the ulcer, and/or diffuse peritonitis for a duration of over 12 hours with fibrous membranes difficult to remove laparoscopically. In the *H. pylori* positive patients, eradication was successful in 96% of the cases. Mortality and morbidity rates were greater in the laparoscopic group ( $p < 0.05$ ). Follow-up (median 43.5 months) revealed no need for reoperation for peptic ulcer disease and no mortality.

**Conclusion:** We have found a high prevalence of *H. pylori* infection in patients with perforated peptic ulcers. An immediate and appropriate *H. pylori* eradication therapy for perforated peptic ulcers reduces the relapse rate after simple closure. Response rate to a triple eradication protocol was excellent in the hospital setting.

**Keywords:** *H. pylori* infection; peptic ulcer disease; perforated ulcers; *H. pylori* eradication; laparoscopic repair

## Introduction

*Helicobacter pylori* (*H. pylori*) infection plays a crucial role in the pathogenesis of peptic ulcer disease. More than 95% of patients suffering from duodenal ulcers and about 70-80% of patients with gastric ulcers are *H. pylori* positive [1, 2]. While there are several reports in the literature [3-6] regarding prevalence of *H. pylori* infection in perforated peptic ulcers, there is a paucity of data from Europe [7, 8]. This study aimed at evaluating prospectively the prevalence of *H. pylori* infection

in patients with acute perforated duodenal or gastric ulcers. In addition, we wanted to evaluate the success rate of *H. pylori* eradication in complicated peptic ulcer disease with a triple treatment regimen. We further analysed outcome, conversion rate, and reasons for conversion in patients with acute perforated peptic ulcers after laparoscopic or open ulcer repair. Laparoscopic perforated ulcer repair has recently been described by many authors [9-15].

## Patients and methods

Between October 1993 and April 1998, all patients diagnosed with acute perforated peptic ulcers were recruited into a prospective study. Demographic data, medical history, past history of previous peptic ulcers, and the use of non-steroidal anti-inflammatory drugs (NSAIDs) were recorded. The protocol required a gastroscopy to be performed in the operating theatre before surgery. Antral biopsies were taken in order to perform a rapid urease test (Campylobacter like organism [CLO] test, DeltaWest Ply, Bentley, Australia) [16]. Intravenous cephalosporin (bolus injection of 1.5 g cefuroxime) was administered at induction of anaesthesia. All patients were treated by either emergency laparoscopy or laparotomy and a simple closure of the perforated ulcer by oversewing. Extensive debridement and cleaning of the peritoneal cavity with several litres of warm sterile saline solution was performed.

Immediately after the operation, an intravenous therapy with ranitidine or omeprazole was initiated. All patients with a positive intraoperative CLO test were started on *H. pylori* eradication therapy when on oral diet. Patients

1–27 (Oct 93–Nov 95) were treated with an eradication regimen consisting of a triple therapy with ranitidine 300 mg each night or omeprazole 40 mg once daily for six weeks, and two antibiotics for 10 days (amoxicillin 750 mg three times daily plus metronidazole 500 mg twice daily). In patients 28–47 (Dec 95–Apr 98) metronidazole was replaced by clarithromycin 500 mg twice daily. The reason for this substitution was the relatively high prevalence of metronidazole-resistant *H. pylori* in our area [17]. For gastric ulcers, gastroscopy was performed six weeks postoperatively to monitor the healing of the ulcer and to exclude a gastric cancer. Patients suffering from a duodenal ulcer did not undergo a follow-up gastroscopy on a regular basis. Six weeks postoperatively, and at least two weeks after the end of the eradication therapy, a <sup>13</sup>C-urea breath test was performed [16] in those patients not having a second endoscopy. Follow-up included a questionnaire regarding persistent symptoms (dyspepsia and reflux symptoms (heartburn)), the need for antacid intake or reoperation for peptic ulcer disease.

## Results

During the 55-month period, 47 patients were enrolled into the study. Their mean age was 64 years (range 27–91 yr). Twenty-nine (62%) were men. Only 11 (23%) had a past history of peptic ulcer disease, and 15 (32%) were taking NSAIDs or steroids. Antral mucosal biopsies were obtained in 45 patients (95.7%). The urease test (CLO) was positive in 33 (73.3%) of these 45 patients. Details of *H. pylori* infected and non-infected patients are summarised in Table 1. Patients with *H. pylori* infection were on average 10 years younger. The

proportion of men in the infected group was 70% compared to 33% in the non-infected group. Type of ulcer, past history of ulcers, current NSAID and steroid intake were similar in both groups (Table 1).

Of the 47 patients, 33 (70.2%) underwent a diagnostic laparoscopy. In 18 (54.5%) out of these 33 patients a laparoscopic suture repair and washout of the peritoneal cavity was successfully performed. Fifteen (32%) were converted to open surgery because of extensive soiling (4-quadrant peri-

**Table 1**

Comparison of the patients with perforated peptic ulcers found to be positive and negative for *Helicobacter pylori* by intraoperative CLO test (n = 45).

	<i>Helicobacter pylori</i> positive 33 (73.3%)	<i>Helicobacter pylori</i> negative 12 (26.7%)	total 45 (100%)
Gastric ulcer	16 (48%)	6 (50%)	22 (48%)
Duodenal ulcer	17 (52%)	6 (50%)	23 (52%)
Sex: ♂ / ♀	23 (70%) / 10 (30%)	4 (33%) / 8 (67%)	27 (60%) / 18 (40%)
Mean age (yr)	61.2	71.7	64
Range (yr)	31–87	27–91	27–91
Past history of peptic ulcers	8 (24%)	3 (25%)	11 (24%)
Current NSAIDs	8 (24%)	3 (25%)	11 (24%)

**Table 2**

Age, sex and complications in relation to operative approach and hospital stay (n = 45).

		laparoscopy	laparotomy	conversion (laparoscopy → laparotomy)
No. of patients		18 (38%)	14 (30%)	15 (32%)
Sex (♂/♀)		13/5	10/4	6/9
Age (mean) yr		61.1	65.4	66.5
Hospital stay (median):	Days	11.5	18	
	Range	5–55	8–54	
	Death	2	0	
Complications:	Intraoperative	1	0	
	Postoperative-local	3	1	
	Postoperative-general	4	2	
	Reoperation	3	1	

**Table 3**

Follow-up of *H. pylori* treated patients (n = 33).

	n	%
Follow-up	24	73%
Reoperation	0	0%
Death	6*	25%
Antacids	1	4%
Symptoms (mild)	3	12.5%
Symptoms (severe)	0	0%
Time (median)	43.5 months	
Range	(10.3 – 65.1 months)	

\* not related to peptic ulcer disease

tonitis) (67%), technical problems during laparoscopic repair (20%), or adhesions (13%). Treatment results, morbidity and mortality data are given in Table 2.

Three patients in the laparoscopic group and one patient in the open surgery group required reoperation. One major complication occurred in the laparoscopic group. An injury of the common bile duct occurred in a 74-year-old woman with a

known metastatic lung cancer. She underwent a laparotomy for cholecystectomy and T-drainage of the common bile duct. Two other patients in the laparoscopic group and one in the open surgery group underwent further surgery due to intra-abdominal infection. Two patients died: the 74-year-old woman having metastatic lung cancer who underwent reoperation for the common bile duct injury, and an 84-year-old woman who died from heart failure on the second postoperative day.

Median hospital stay was longer for the open surgery group (18 days) versus the laparoscopic group (12 days) ( $p < 0.05$ ).

Twenty-seven (82%) out of 33 patients who had a positive intraoperative CLO test underwent a  $^{13}\text{C}$ -urea breath test or a gastroscopy including a CLO test 6 weeks postoperatively. By that time 26 patients were *H. pylori* negative, giving a success rate of *H. pylori* eradication of 96%.

We were able to follow 24 of the 33 patients (73%) who were initially treated for *H. pylori* infection. Table 3 gives the results of this follow-up.

## Discussion

In the 45 patients presenting with acute perforation of a gastric or duodenal ulcer, the prevalence of *H. pylori* was 73.3%. In contrast with the literature, we found roughly the same incidence of *H. pylori* infection for both gastric and duodenal ulcers.

Data regarding *H. pylori* infection in perforated peptic ulcers are conflicting. Indeed, *H. pylori* infection rates range from 0 to 92 per cent [3–5, 7, 8, 18–21] (see also table 4). Some reports show that eradication of *H. pylori* can prevent recurrent ulcer disease complications such as bleeding [10, 22]. This has been demonstrated recently by Ng et al. [4] in perforated peptic ulcers. These authors showed in a randomised clinical trial that eradication of *H. pylori* prevents ulcer recurrence in patients with *H. pylori*-associated perforated duodenal ulcers. Of 99 *H. pylori* positive patients, 51 were assigned to an anti-*H. pylori* therapy, and 48 to omeprazole alone. After one year, ulcer relapse was significantly lower in patients treated with an anti-*H. pylori* therapy (4.8 vs. 38.1%). Likewise, Chu et al. [5] concluded that recurrent ulcer disease in pa-

tients with a history of perforated duodenal ulcer is related to *H. pylori* infection. None of our patients had to undergo repeated surgery for recurrent peptic ulcer disease after simple closure of perforated ulcer and successful *H. pylori* eradication. The discrepancy between infection rates found in the literature [3–5, 7, 8, 18–21] may be attributed in part to the different populations studied. For example, Sebastian et al. [7] reported an infection rate of 83% in a small group of young male smokers from India with acute perforated peptic ulcers; this result is comparable to our findings. Another small study from India [21] with 15 perforated duodenal ulcer patients showed on the contrary that all patients were negative for *H. pylori*; while Sharma et al. [3] found a prevalence of 61% among 44 patients from Chattisgarh region, India. Reinbach et al. [8] claimed that perforated ulcers might have a different pathogenesis because in their study only 47% of the perforated duodenal ulcer patients were positive for *H. pylori*. Forty-four per cent of their patients were on NSAIDs, and their study showed no difference between NSAID users and non-users in relation to *H. pylori* infection. Another study described similar results [20]. Matsukura et al. [23] showed that there were no significant differences between perforated and non-surgical peptic ulcer groups for *H. pylori* serum and gene markers. Ng et al. [18] on the other hand found a 70% infection rate (n = 73) in perforated duodenal or prepyloric ulcer patients; their figures are similar to ours. This is barely higher than the prevalence of *H. pylori* infection in the local population, and obviously lower than would be expected among patients with duodenal ulcers.

**Table 4**

Prevalence of *Helicobacter pylori* infection in patients with perforated peptic ulcers.

Author	year	No patients	<i>H. p.</i> positive (%)
Reinbach [8]	1993	80	47%
Sebastian [7]	1995	29	83%
Debonnie [20]	1995	36	56%
Ng [18]	1996	73	70%
Chowdhary [21]	1998	15	0%
Chu [5]	1999	163	47%
Ng [4]	2000	129	81%
Sharma [3]	2000	44	61%

In patients not on NSAIDs they found an 80% infection rate. We, on the contrary found no difference in the *H. pylori* infection rate between the two groups of NSAID users and non-users.

It would be beyond the scope of this paper to discuss the different *H. pylori* eradication regimens and their success rate. Our eradication rate of 96% is excellent [24, 25]. Most of our patients had a significant part of their eradication therapy on an inpatient basis due to the long hospital stay required for the procedure. Therefore we consider patient compliance as an important factor for a successful treatment. This is confirmed by previous findings [26].

While elective ulcer surgery declines significantly, the percentage of emergency operations for complicated ulcers has recently increased from 60 to 90% [19]. Simple closure of perforations gained popularity in the presence of potent acid-suppressing and *H. pylori* eradication agents [27–29]. Despite a high recurrence rate of up to 40% after simple suture of a perforated ulcer [30, 31], definitive acid-reduction ulcer surgery is on the decrease. The high age of the patient population with its comorbidity, and the availability of efficient *H. pylori* eradication regimens may account for this move away from extensive surgery [32, 33].

A variety of laparoscopic techniques for closure of perforated peptic ulcers have recently emerged [34–37].

Lau et al. [33] carried out a randomised study comparing laparoscopic versus open surgery for perforated peptic ulcers. They reported that laparoscopic repair followed by peritoneal washout had become standard treatment. They found no significant difference in morbidity, reoperating rate, and mortality between laparoscopic or open repair. Hospital stay and time needed to resume normal activity was similar in both groups. In contrast with elective laparoscopic surgery such as cholecystectomy or fundoplication, patients do not seem to benefit from a less invasive approach. The main complications of acute perforated peptic ulcers are the consequences of peritonitis, development of septicaemia and reduced gastrointestinal motility. Therefore, irrespective of the way in which the perforation is repaired, patients probably need the same period of time to recover [33].

Nonetheless, due to cost restraints in the health care system, decreasing hospital stay may become a major issue all over Europe. However, optimal treatment of the total peritoneal surface is essential if abscess formation within the abdominal cavity is to be avoided as much as possible. Hence, open surgery may be needed, especially if the perforation has been persisting for some hours.

In comparison, our conversion rate was extremely high: 32%. To our knowledge two main factors were responsible for this. First, callous ulcers greater than 1 centimetre in diameter are difficult to close by a laparoscopic approach especially if there is a need for additional excision, as is the case for gastric ulcers. Second, in cases of peritonitis persisting for over 24 hours, we found it easier to perform an adequate cleaning of the peritoneal cavity by an open approach.

Recently, Katkhouda et al. [38] showed that laparoscopy is not beneficial in patients with large perforations (diameter >6 mm), or patients in shock. Lee et al. [39] noticed a conversion rate of 27% in the laparoscopic group. According to their findings, large ulcers (diameter > 10 mm) and high APACHE II scores were risk factors in laparoscopic repair.

In summary, this study shows that there is an evident association between *H. pylori* infection and acute perforated peptic ulcers, regardless of chronic NSAID use. A Triple *H. pylori* eradication regimen in a hospital setting is successful and yields a response rate of 96%.

We conclude from these results, that *H. pylori* infection status should be assessed at the initial endoscopy or operation, regardless of concomitant NSAID intake. If *H. pylori* infection is found, an appropriate eradication therapy should be initiated as soon as possible.

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